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COLLEGE OF MEDICINE
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Dr. Joshua Lederberg
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Dear Dr. Lederberg:

I returned from abroad a week ago and found your letter waiting. I have the impression that you would not object to a continuation of our dialogue.

I did see your column of 11/29/69 and paragraphs 4 and 5 are pertinant to the statement I made in my letter to you. You may recall the case of Agene, NCl_3. This bread softener was taken off the market when it was found that large, repetitive doses caused "running fits" in dogs. This occurred prior to the Delaney Bill. At that time, a food additive could (not must) be withdrawn if any harm at any dose was shown. NCl_3 was withdrawn. The Delaney Bill changed this very deliberately, so that if a food additive was shown to safe under the intended conditions of use, it was permitted to be used. In practice, under the regulations, not the statute, this meant establishing a no-effect level in chronic tests with a rodent (usually rats) and a non-rodent (usually dosgs) species. The intended use level needed to be at least at the no-effect level, and in practice, the use level was arbitrarily set at 100X below the no-effect level. Under the Delaney Bill, Agene might still be on the market, because among other things, the effect on dogs was due to the dogs' peculiar metabolism. Basically, recognition was given to the pharmacolgical, or dose-response, characteristics of food additive chemicals.

The objectionable thing in the FDA procedures, as I pointed out in my previous letter, is the arbitrary safety limit. It is scientifically irrational, and may be too small or too large. But regardless; if the Delaney Bill recognizes that there may be an effective no-effect level for liver damage, kidney damage, demyelination, etc, then the same shoud apply to carcinogens, on the assumption that they act pharmacologically. Of course, if it should be shown that all cancers are viral-induced, then all bets are off. You would choose demyelination over cancer (if you had your druthers). I don't think your choice is a good one, the undesirability of each notwithstanding. Many cancers are amenable to treatment - demyelination is not.

You argue that other potential hazards are not considered under the Delaney Bill (Safety Standards for Envoirnmental Hazards, 11/30/69). The Bill is concern- only with food additives, and should not be taken to task for not overseeing other envoirnmental hazards. In terms of food additives, the Bill does, however, consider chronic diseases on the basis of establishing a no-effect level, but it does not do so in terms of preexisting disease. The development of a chronic condition or of iatrogenic disease, is definitely sought in chronic test. I would also point out that it is 2-3 years since "zero tolerances " were used. Presently decisions are made on the basis of "negligible residues" for precisely

the reasons you stated. But neither zero tolerance nor neglible residues are the same as no-effect. This change in residue levels, incidentally, was an administrative change in the regulations, and was not a change in the statute.

Basically then, I argue that if carcinogens act pharmacologically, then they should be treated as other pharmacologically active substances, and a no-effect level should be established. You argue that pharmacolgically active substances, regardless of carcinogeneity, be banned if they are found to cause disease in any animal at any dose (ref.supra), a situation which the Delaney Bill deliberately avoided.

The last sentence in the referred article is of course, the same as my argument that an arbitrary safety limit is not scientific: but scientific standards are possible, and should be established, but they should be established on the basis of 10^{-6} <u>effect</u> and not on 10^{-6} dose, as is presently done.

Sincerely,

Frederick Sperling